



General

Guideline Title

Acute upper gastrointestinal bleeding: management.

Bibliographic Source(s)

National Institute for Health and Clinical Excellence (NICE). Acute upper gastrointestinal bleeding: management. London (UK): National Institute for Health and Clinical Excellence (NICE); 2012 Jun. 23 p. (Clinical guideline; no. 141).

Guideline Status

This is the current release of the guideline.

The National Institute for Health and Clinical Excellence (NICE) reaffirmed the currency of this guideline in 2014.

Regulatory Alert

FDA Warning/Regulatory Alert

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- [December 14, 2016 – General anesthetic and sedation drugs](#) : The U.S. Food and Drug Administration (FDA) is warning that repeated or lengthy use of general anesthetic and sedation drugs during surgeries or procedures in children younger than 3 years or in pregnant women during their third trimester may affect the development of children's brains. Consistent with animal studies, recent human studies suggest that a single, relatively short exposure to general anesthetic and sedation drugs in infants or toddlers is unlikely to have negative effects on behavior or learning. However, further research is needed to fully characterize how early life anesthetic exposure affects children's brain development.

Recommendations

Major Recommendations

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Clinical Guideline Centre (NCGC) on behalf of the National Institute for Health and Clinical Excellence (NICE) (see the "Availability of Companion Documents" field for the full version of this guidance).

Risk Assessment

Use the following formal risk assessment scores for all patients with acute upper gastrointestinal bleeding:

- Blatchford score at first assessment, and
- Full Rockall score after endoscopy

Consider early discharge for patients with a pre-endoscopy Blatchford score of 0.

Resuscitation and Initial Management

Transfuse patients with massive bleeding with blood, platelets and clotting factors in line with local protocols for managing massive bleeding.

Base decisions on blood transfusion on the full clinical picture, recognising that over-transfusion may be as damaging as under-transfusion.

Do not offer platelet transfusion to patients who are not actively bleeding and are haemodynamically stable.

Offer platelet transfusion to patients who are actively bleeding and have a platelet count of less than $50 \times 10^9/\text{litre}$.

Offer fresh frozen plasma to patients who have either:

- Fibrinogen level of less than 1 g/litre, or
- Prothrombin time (international normalised ratio) or activated partial thromboplastin time greater than 1.5 times normal

Offer prothrombin complex concentrate to patients who are taking warfarin and actively bleeding.

Treat patients who are taking warfarin and whose upper gastrointestinal bleeding has stopped in line with local warfarin protocols.

Do not use recombinant factor VIIa except when all other methods have failed.

Timing of Endoscopy

Offer endoscopy to unstable patients with severe acute upper gastrointestinal bleeding immediately after resuscitation.

Offer endoscopy within 24 hours of admission to all other patients with upper gastrointestinal bleeding.

Units seeing more than 330 cases a year should offer daily endoscopy lists. Units seeing fewer than 330 cases a year should arrange their service according to local circumstances.

Management of Non-Variceal Bleeding

Endoscopic Treatment

Do not use adrenaline as monotherapy for the endoscopic treatment of nonvariceal upper gastrointestinal bleeding.

For the endoscopic treatment of non-variceal upper gastrointestinal bleeding, use one of the following:

- A mechanical method (for example, clips) with or without adrenaline
- Thermal coagulation with adrenaline
- Fibrin or thrombin with adrenaline

Proton Pump Inhibitors

Do not offer acid-suppression drugs (proton pump inhibitors or H_2 -receptor antagonists) before endoscopy to patients with suspected non-variceal upper gastrointestinal bleeding.

Offer proton pump inhibitors to patients with non-variceal upper gastrointestinal bleeding and stigmata of recent haemorrhage shown at endoscopy.

Treatment after First or Failed Endoscopic Treatment

Consider a repeat endoscopy, with treatment as appropriate, for all patients at high risk of re-bleeding, particularly if there is doubt about adequate haemostasis at the first endoscopy.

Offer a repeat endoscopy to patients who re-bleed with a view to further endoscopic treatment or emergency surgery.

Offer interventional radiology to unstable patients who re-bleed after endoscopic treatment. Refer urgently for surgery if interventional radiology is not promptly available.

Management of Variceal Bleeding

Offer terlipressin to patients with suspected variceal bleeding at presentation. Stop treatment after definitive haemostasis has been achieved, or after 5 days, unless there is another indication for its use.*

Offer prophylactic antibiotic therapy at presentation to patients with suspected or confirmed variceal bleeding.

*At the time of publication (June 2012), terlipressin was indicated for the treatment of bleeding from oesophageal varices, with a maximum duration of treatment of 72 hours (3 days). Prescribers should consult the relevant summary of product characteristics. Informed consent for off-label use of terlipressin should be obtained and documented.

Oesophageal Varices

Use band ligation in patients with upper gastrointestinal bleeding from oesophageal varices.

Consider transjugular intrahepatic portosystemic shunts (TIPS) if bleeding from oesophageal varices is not controlled by band ligation.

Gastric Varices

Offer endoscopic injection of *N*-butyl-2-cyanoacrylate to patients with upper gastrointestinal bleeding from gastric varices.

Offer TIPS if bleeding from gastric varices is not controlled by endoscopic injection of *N*-butyl-2-cyanoacrylate.

Control of Bleeding and Prevention of Re-Bleeding in Patients on Non-steroidal Anti-inflammatory Drugs (NSAIDs), Aspirin or Clopidogrel

Continue low-dose aspirin for secondary prevention of vascular events in patients with upper gastrointestinal bleeding in whom haemostasis has been achieved.

Stop other non-steroidal anti-inflammatory drugs (including cyclooxygenase-2 [COX-2] inhibitors) during the acute phase in patients presenting with upper gastrointestinal bleeding.

Discuss the risks and benefits of continuing clopidogrel (or any other thienopyridine antiplatelet agents) in patients with upper gastrointestinal bleeding with the appropriate specialist (for example, a cardiologist or a stroke specialist) and with the patient.

Primary Prophylaxis for Acutely Ill Patients in Critical Care

Offer acid-suppression therapy (H₂-receptor antagonists or proton pump inhibitors) for primary prevention of upper gastrointestinal bleeding in acutely ill patients admitted to critical care. If possible, use the oral form of the drug.

Review the ongoing need for acid-suppression drugs for primary prevention of upper gastrointestinal bleeding in acutely ill patients when they recover or are discharged from critical care.

Information and Support for Patients and Carers

Establish good communication between clinical staff and patients and their family and carers at the time of presentation, throughout their time in hospital and following discharge. This should include:

- Giving verbal information that is recorded in medical records
- Different members of clinical teams providing consistent information
- Providing written information where appropriate
- Ensuring patients and their families and carers receive consistent information

Clinical Algorithm(s)

The recommendations from this guideline have been incorporated into a [NICE pathway](#) .

Scope

Disease/Condition(s)

Acute variceal and non-variceal upper gastrointestinal bleeding

Guideline Category

Diagnosis

Evaluation

Management

Prevention

Risk Assessment

Treatment

Clinical Specialty

Anesthesiology

Critical Care

Emergency Medicine

Gastroenterology

Radiology

Surgery

Intended Users

Advanced Practice Nurses

Nurses

Patients

Pharmacists

Physician Assistants

Physicians

Guideline Objective(s)

- To identify which diagnostic and therapeutic steps are useful in managing acute upper gastrointestinal bleeding
- To enable hospitals to develop a structure in which clinical teams can deliver an optimum service for people who develop this condition
- To offer best practice advice on the care of adults and young people aged 16 years and older with acute variceal and non-variceal upper gastrointestinal bleeding

Target Population

- Adults and young people (16 years and older) with acute variceal and non-variceal upper gastrointestinal bleeding
- Adults and young people in high dependency and intensive care units who are at high risk of acute upper gastrointestinal bleeding

The guideline excludes:

- Adults with chronic upper gastrointestinal bleeding
- Children (15 years and below)
- Patients with a bleeding point lower than the duodenum

Interventions and Practices Considered

1. Risk assessment:
 - Blatchford score
 - Rockall score
2. Resuscitation and initial management
 - Transfusion of blood, platelets and clotting factors
 - Fresh frozen plasma
 - Prothrombin complex concentrate
 - Recombinant factor VIIa
 - Management of patients on warfarin
3. Endoscopy
4. Management of non-variceal bleeding
 - Endoscopic treatment (mechanical method with or without adrenaline, thermal coagulation with adrenaline, fibrin or thrombin with adrenaline)
 - Use of proton pump inhibitors
 - Repeat endoscopy
 - Interventional radiology
5. Management of variceal bleeding
 - Terlipressin
 - Prophylactic antibiotic therapy
 - Band ligation
 - Transjugular intrahepatic portosystemic shunts (TIPS)
6. Control of bleeding and prevention of re-bleeding in patients on non-steroidal anti-inflammatory drugs (NSAIDs), aspirin or clopidogrel
7. Primary prophylaxis for acutely ill patients in critical care (acid suppression therapy)
8. Provision of information and support for patients and carers

Major Outcomes Considered

- Mortality
- Re-bleeding
- Need for surgery or other interventions
- Blood transfusion requirements
- Length of hospital stay
- Health-related quality of life
- Adverse effects
- Cost-effectiveness

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Clinical Guideline Centre (NCGC) on behalf of the National Institute for Health and Clinical Excellence (NICE) (see the "Availability of Companion Documents" field for the full version of this guidance).

Searching for Evidence

Clinical Literature Search

Systematic literature searches were undertaken to identify evidence within published literature in order to answer the review questions as per The Guidelines Manual (see the "Availability of Companion Documents" field). Clinical databases were searched using relevant medical subject headings, free-text terms and study type filters where appropriate. Studies published in languages other than English were not reviewed. Where possible, searches were restricted to articles published in English language. All searches were conducted on core databases, MEDLINE, Embase, Cinahl and The Cochrane Library. Additional subject specific databases were used for some questions: e.g., PsycInfo for patient experience. All searches were updated on September 23, 2011. No papers after this date were considered.

Search strategies were checked by looking at reference lists of relevant key papers, checking search strategies in other systematic reviews and asking the Guideline Development Group (GDG) for known studies. The questions, the study types applied, the databases searched and the years covered can be found in Appendix C of the full guideline document (see the "Availability of Companion Documents" field).

During the scoping stage, a search was conducted for guidelines and reports on the websites listed below and on organisations relevant to the topic. Searching for grey literature or unpublished literature was not undertaken. All references sent by stakeholders were considered.

- Guidelines International Network database (www.g-i-n.net)
- National Guideline Clearinghouse (www.guideline.gov/)
- National Institute for Health and Clinical Excellence (NICE) (www.nice.org.uk)
- National Institutes of Health Consensus Development Program (consensus.nih.gov/)
- National Library for Health (www.library.nhs.uk/)

Health Economic Literature Search

Systematic literature searches were also undertaken to identify health economic evidence within published literature relevant to the review questions. The evidence was identified by conducting a broad search relating to the guideline population in the National Health Service Economic Evaluation Database (NHS EED), the Health Economic Evaluations Database (HEED) and Health Technology Assessment (HTA) databases with no date restrictions. Additionally, the search was run on MEDLINE and Embase, with a specific economic filter, from 2009, to ensure recent publications that had not yet been indexed by these databases were identified. Where possible, searches were restricted to articles published in English language.

The search strategies for health economics are included in Appendix C of the full guideline document (see the "Availability of Companion Documents" field). All searches were updated on July 23, 2011. No papers published after this date were considered.

Evidence of Effectiveness

The Research Fellow:

- Identified potentially relevant studies for each review question from the relevant search results by reviewing titles and abstracts – full papers were then obtained.
- Reviewed full papers against pre-specified inclusion/exclusion criteria to identify studies that addressed the review question in the appropriate population and reported on outcomes of interest (review protocols are included in Appendix D of the full guideline document).
- Critically appraised relevant studies using the appropriate checklist as specified in The Guidelines Manual.
- Extracted key information about the study's methods and results into evidence tables (evidence tables are included in Appendix F of the full guideline document).
- Generated summaries of the evidence by outcome (included in the relevant chapter write-ups):
 - Randomised studies: meta-analysed, where appropriate and reported in Grading of Recommendations Assessment, Development and Evaluation (GRADE) profiles (for clinical studies)

- Observational studies: data presented as a range of values in GRADE profiles
- Diagnostic studies: data presented as a range of values in adapted GRADE
- Qualitative studies: each study summarised in a table where possible, otherwise presented in a narrative
- Fifteen percent of the sift and checklists as well as whole reviews were quality assured by a second reviewer to eliminate any potential of section bias or error.

Inclusion/Exclusion

The inclusion/exclusion of studies was based on the review protocols. The GDG were consulted about any uncertainty regarding inclusion/exclusion of selected studies. With regards to review question 16 the GDG agreed that studies with a mixed patient population, i.e., patients with gastric varices and also patients with oesophageal varices should be permitted as indirect evidence. The GDG agreed that there was insufficient evidence if this was restricted to studies entirely of patients with gastric variceal bleeding.

Patients bleeding from upper gastrointestinal (GI) varices due to schistosomiasis were excluded since the cause of bleeding compared to those patients bleeding due to cirrhosis of the liver. Schistosomiasis is a parasitic illness originating from Africa and is uncommon in the United Kingdom (UK).

In the antibiotic review question (question 19) erythromycin was excluded since this is used in a different clinical context to that specified in the review question.

See the review protocols in Appendix D of the full guideline document (see the "Availability of Companion Documents" field) for full details.

Type of Studies

Systematic reviews, triple blinded, double blinded, single blinded and unblinded parallel randomised controlled trials (RCTs) as well as observational studies were included in the evidence reviews for this guideline. Randomised trials were included, as they are considered the most robust type of study design that could produce an unbiased estimate of the intervention effects.

The GDG decided to include observational studies in questions where ethical considerations would not permit randomisation. These were for the question regarding resuscitation with blood products (questions 7 and 8) and for the question assessing the treatment options when the bleeding remained uncontrolled after first line intervention (question 12). Randomised control trials are not the appropriate study type for risk assessment test accuracy analysis. For this review (question 3) prospective as well as retrospective case reviews were analysed.

Evidence of Cost-Effectiveness

Inclusion/Exclusion

Full economic evaluations (studies comparing costs and health consequences of alternative courses of action: cost-utility, cost-effectiveness, cost-benefit and cost-consequence analyses) and comparative costing studies that addressed the review question in the relevant population were considered potentially applicable as economic evidence.

Studies that only reported cost per hospital (not per patient), or only reported average cost effectiveness without disaggregated costs and effects, were excluded. Abstracts, posters, reviews, letters/editorials, foreign language publications and unpublished studies were excluded. Studies judged 'not applicable' were excluded (this included studies that took the perspective of a non-Organisation for Economic Cooperation and Development [OECD] country).

Remaining studies were prioritised for inclusion based on their relative applicability to the development of this guideline and the study limitations. For example, if a high quality, directly applicable UK analysis was available other less relevant studies may not have been included. Where exclusions occurred on this basis, this is noted in the relevant section.

For more details about the assessment of applicability and methodological quality see the economic evaluation checklist (The Guidelines Manual, Appendix H) and the health economics research protocol in Appendix D of the full guideline document (see the "Availability of Companion Documents" field).

When no relevant economic analysis was found from the economic literature review, relevant UK NHS unit costs related to the compared interventions were presented to the GDG to inform the possible economic implication of the recommendation to make.

2014 Reaffirmation

NICE Evidence Update 63 provides a summary of selected new evidence published since the literature search was last

conducted. The Evidence Update gives a preliminary assessment of changes in the evidence base and a final decision on whether the guidance should be updated is made by NICE according to its published processes and methods. For contextual information, the Evidence Update should be read in conjunction with the relevant clinical guideline. Evidence Updates are intended to increase awareness of new evidence – they do not replace current NICE guidance and do not provide formal practice recommendations.

Number of Source Documents

See Appendix E: Clinical Study Selection Flow Charts in the Appendices section of the full guidance (see the "Availability of Companion Documents" field).

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Overall Quality of Outcome Evidence in GRADE (Grading of Recommendations Assessment, Development and Evaluation)

Level	Description
High	Further research is very unlikely to change confidence in the estimate of effect
Moderate	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate
Low	Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate
Very Low	Any estimate of effect is very uncertain

Methods Used to Analyze the Evidence

Meta-Analysis

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Clinical Guideline Centre (NCGC) on behalf of the National Institute for Health and Clinical Excellence (NICE) (see the "Availability of Companion Documents" field for the full version of this guidance).

Methods of Combining Clinical Studies

Data Synthesis for Intervention Reviews

Where possible, meta-analyses were conducted to combine the results of studies for each review question using Cochrane Review Manager (RevMan5) software. Fixed-effects (Mantel-Haenszel) techniques were used to calculate risk ratios (relative risk) for binary outcomes. Continuous outcomes were analysed using an inverse variance method for pooling weighted mean differences and where the studies had different scales, standardised mean differences were used. Where reported, time-to-event data was presented as a hazard ratio.

Statistical heterogeneity between individual study results in a meta-analysis was assessed by considering the Chi-squared test for significance at $p < 0.1$ or an I-squared inconsistency statistic of $> 50\%$ to indicate significant heterogeneity. Where significant heterogeneity was present, reviewers carried out predefined subgroup analyses for length of follow-up, severity of cirrhosis (for groups of patients with variceal bleeding), severity of illness in intensive care/high dependency patients (question 15). Intravenous and oral drug administration of proton pump inhibitors (question 2) and type of combination treatment (question 18) were a priori subgroups due to the specific nature of the questions.

Assessments of potential differences in effect between subgroups were based on the Chi-squared tests for heterogeneity statistics between subgroups. If no subgroup analysis was found to completely resolve statistical heterogeneity then a random effects (DerSimonian and Laird) model was employed to provide a more conservative estimate of the effect.

The means and standard deviations of continuous outcomes were required for meta-analysis. However, in cases where standard deviations were not reported, the standard error was calculated if the p-values or 95% confidence intervals were reported and meta-analysis was undertaken with the mean and standard error using the generic inverse variance method in Cochrane Review Manager (RevMan5) software. Where p values were reported as "less than", a conservative approach was undertaken. For example, if p value was reported as " $p \leq 0.001$ ", the calculations for standard deviations will be based on a p value of 0.001.

For binary outcomes, absolute event rates were also calculated using the GRADEpro software using event rate in the control arm of the pooled results.

Data and Outcomes

In studies for the risk assessment review all patients received a formal risk assessment which was then scored according to the particular system(s) under investigation. Patients could then be categorised into those that scored above or below a clinically specified cut-off points (as described in more detail in chapter 5 of the full version of the original guideline. This allowed reviewers to extract the proportion of those above and those below the cut-off who experienced a particular outcome. From this reviewers derived components of "2x2 tables" (true positives, false positives, true negatives and false negatives) and then calculated accuracy parameters: sensitivity, specificity, positive/negative predictive value and positive/negative likelihood ratios. For some studies areas under curve of a receiver operating characteristics curve (AUC, which is another accuracy measure) was also extracted. When data were only graphical presented (with sufficient levels of detail), frequencies were extracted from the figures to create 2x2 tables (this is noted in the extraction Tables in section 2 of Appendix F of the full version of the original guideline document).

Data Synthesis for Risk Assessment Data

When data from 5 or more studies were available, a diagnostic meta-analysis was carried out. Graphs of point estimates for sensitivity and specificity with 95% confidence intervals were presented side-by-side for individual studies using Cochrane Review Manager (RevMan5) software. To show the differences between study results on graphical space, pairs of sensitivity and specificity were plotted for each study on one receiver operating characteristics (ROC) curve in Microsoft EXCEL software (for RevMan5 and Excel plots please see Appendix L of the full version of the original guideline document). Study results were pooled using the bivariate method for the direct estimation of summary sensitivity and specificity using a random effects approach (in WinBUGS® software - for the program code see Appendix L of the full version of the original guideline document). This model also assesses the variability by incorporating the precision with which sensitivity and specificity have been measured in each study. A confidence ellipse is shown in the graph that indicates the confidence region around the summary sensitivity/specificity point. A summary ROC curve is also presented. From the WinBUGS® output the summary estimate of sensitivity and specificity (plus their standard deviations) are reported in the graphical presentation of the meta-analysis results. The bivariate meta-analysis method is described in more detail in Appendix L of the full version of the original guideline document.

Type of Analysis

Estimates of effect from individual studies were based on intention-to-treat (ITT) analysis with the exception of the outcome of experience of adverse events where available case analysis (ACA) was used. ITT analysis is where all participants included in the randomisation process were considered in the final analysis based on the intervention and control groups to which they were originally assigned. It was assumed that participants in the trials lost to follow-up did not experience the outcome of interest (for categorical outcomes) and they would not considerably change the average scores of their assigned groups (for quantitative outcomes).

It is important to note that ITT analyses tend to bias the results towards no difference. ITT analysis is a conservative approach to analyse the data, and therefore the effect may be smaller than in reality. However, the majority of outcomes selected to be reviewed were continuous outcomes, very few people dropped out and most of the studies reported data on an ITT basis.

Appraising the Quality of Evidence by Outcomes

The evidence for outcomes from the included RCT and observational studies were evaluated and presented using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group (<http://www.gradeworkinggroup.org/>). The software (GRADEpro) developed by the GRADE working group was used to assess the quality of each outcome, taking into account individual study quality and the meta-analysis results. The summary of findings is presented in landscape tables in the full version of the original guideline. The GRADE summary table includes details of the quality assessment as

well as pooled outcome data, where appropriate, an absolute measure of intervention effect and the summary of quality of evidence for that outcome. For binary outcomes such as number of patients with an adverse event, the event rates (n/N: number of patients with events divided by sum of number of patients) are shown with percentages. Reporting or publication bias was only taken into consideration in the quality assessment and included in the Clinical Study Characteristics table if it was apparent. Each outcome was examined separately for the quality elements listed and defined in Table 1 of the full version of the guideline and each graded using the quality levels listed in Table 2 of the full guideline. The main criteria considered in the rating of these elements are discussed below. Footnotes were used to describe reasons for grading a quality element as having serious or very serious problems. The ratings for each component were summed to obtain an overall assessment for each outcome.

Grading the Quality of Clinical Evidence

After results were pooled, the overall quality of evidence for each outcome was considered (see the "Rating Scheme for the Strength of the Evidence" field). The following procedure was adopted when using Grading of Recommendations Assessment, Development and Evaluation (GRADE):

1. A quality rating was assigned, based on the study design. RCTs start HIGH and observational studies as LOW, uncontrolled case series as LOW or VERY LOW.
2. The rating was then downgraded for the specified criteria: Study limitations, inconsistency, indirectness, imprecision and reporting bias. These criteria are detailed in the full version of the original guideline. Observational studies were upgraded if there was: a large magnitude of effect, dose-response gradient, and if all plausible confounding would reduce a demonstrated effect or suggest a spurious effect when results showed no effect. Each quality element considered to have "serious" or "very serious" risk of bias was rated down -1 or -2 points respectively.
3. The downgraded/upgraded marks were then summed and the overall quality rating was revised. For example, all RCTs started as HIGH and the overall quality became MODERATE, LOW or VERY LOW if 1, 2 or 3 points were deducted respectively.
4. The reasons or criteria used for downgrading were specified in the footnotes.

Adaptation of GRADE for Risk Scoring Outcomes

GRADE rating tables were adapted for this review. In the first section they were presented for each risk assessment system and each outcome. Another adapted GRADE table is presented for the results of the diagnostic meta-analyses for which outcomes of some of the pre-endoscopy scoring systems were combined.

Compared to intervention studies, in risk scoring assessment studies different study designs and statistics are appropriate. Therefore the intervention GRADE table was adapted for this review to reflect these differences. For each risk outcome (mortality, rebleeding and need for intervention) results were summarised across studies. For each a range of sensitivity, specificity, positive/negative predictive value, negative likelihood ratio and area under curve were reported. The aspects of GRADE were then assessed across studies. Currently no standard risk of bias checklist is used for these types of studies at the NCGC. Study limitations were assessed by considering patient selection. These were: retrospective study design, representativeness of study population, study population size, whether all patients received the assessment and how much loss to follow-up was reported and whether or what type of validation sample was used in the development of the rating system). Imprecision was downgraded whenever there was a difference in the range of reported diagnostic statistics that was $\geq 10\%$.

For data in the diagnostic meta-analyses study limitations were assessed according to the same criteria. Inconsistency was assessed by inspection of the sensitivity/specificity plots and imprecision was rated according to the confidence region of the summary plots (please see Appendix L in the full guideline document).

Additional information related to factors that affect quality such as study limitations, inconsistency, indirectness and imprecision are detailed in the full guideline document.

Evidence of Cost-Effectiveness

The Health Economist:

- Identified potentially relevant studies for each review question from the economic search results by reviewing titles and abstracts – full papers were then obtained.
- Reviewed full papers against pre-specified inclusion/exclusion criteria to identify relevant studies.
- Critically appraised relevant studies using the economic evaluations checklist as specified in The Guidelines Manual.
- Extracted key information about the study's methods and results into evidence tables (evidence tables are included in Appendix G of the full guideline document).
- Generated summaries of the evidence in NICE economic evidence profiles (included in the relevant chapter write-ups in the full guideline document).

document).

NICE Economic Evidence Profiles

The NICE economic evidence profile has been used to summarise cost and cost-effectiveness estimates. The economic evidence profile shows, for each economic study, an assessment of applicability and methodological quality, with footnotes indicating the reasons for the assessment. These assessments were made by the health economist using the economic evaluation checklist from The Guidelines Manual, Appendix H6. It also shows incremental costs, incremental outcomes (for example, quality-adjusted life-years [QALYs]) and the incremental cost-effectiveness ratio from the primary analysis, as well as information about the assessment of uncertainty in the analysis. If a non-UK study was included in the profile, the results were converted into pounds sterling using the appropriate purchasing power parity.

Where economic studies compare multiple strategies, results are generally presented in the economic evidence profiles as an incremental analysis where possible. This is where an intervention is compared with the next most expensive non-dominated option – a clinical strategy is said to 'dominate' the alternatives when it is both more effective and less costly. Otherwise results were presented for the pair-wise comparison specified in the review question.

Undertaking New Health Economic Analysis

As well as reviewing the published economic literature for each review question, as described above, new economic analysis was undertaken by the Health Economist in priority areas. Priority areas for new health economic analysis were agreed by the GDG after formation of the review questions and consideration of the available health economic evidence.

Additional data for the analysis was identified as required through additional literature searches undertaken by the Health Economist, and discussion with the GDG. Model structure, inputs and assumptions were explained to and agreed by the GDG members during meetings, and they commented on subsequent revisions.

See Appendix I and J of the full version of the original guideline for details of the health economic analysis/analyses undertaken for the guideline.

Cost-effectiveness Criteria

NICE's report 'Social value judgements: principles for the development of NICE guidance' sets out the principles that GDGs should consider when judging whether an intervention offers good value for money.

In general, an intervention was considered to be cost effective if either of the following criteria applied (given that the estimate was considered plausible):

- a. The intervention dominated other relevant strategies (that is, it was both less costly in terms of resource use and more clinically effective compared with all the other relevant alternative strategies), or
- b. The intervention cost less than £20,000 per quality-adjusted life-year (QALY) gained compared with the next best strategy.

If the GDG recommended an intervention that was estimated to cost more than £20,000 per QALY gained, or did not recommend one that was estimated to cost less than £20,000 per QALY gained, the reasons for this decision are discussed explicitly in the 'from evidence to recommendations' section of the relevant chapter with reference to issues regarding the plausibility of the estimate or to the factors set out in the 'Social value judgements: principles for the development of NICE guidance.'

Methods Used to Formulate the Recommendations

Expert Consensus

Informal Consensus

Description of Methods Used to Formulate the Recommendations

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Clinical Guideline Centre (NCGC) on behalf of the National Institute for Health and Clinical Excellence (NICE) (see the "Availability of Companion Documents" field for the full version of this guidance).

Developing Recommendations

Over the course of the guideline development process, the Guideline Development Group (GDG) was presented with:

- Evidence tables of the clinical and economic evidence reviewed from the literature. All evidence tables are in Appendices F and G of the full guideline document
- Summary of clinical and economic evidence and quality (as presented in chapters 5-12 of the full guideline document)
- Forest plots and summary receiver-operated characteristic (ROC) curves (Appendix H of the full guideline document)
- A description of the methods and results of the cost-effectiveness analysis undertaken for the guideline (Appendices I and J of the full guideline document)
- Recommendations were drafted on the basis of the GDG interpretation of the available evidence, taking into account the balance of benefits, harms and costs. When clinical and economic evidence was of poor quality, conflicting or absent, the GDG drafted recommendations based on their expert opinion. The considerations for making consensus based recommendations include the balance between potential harms and benefits, economic or implications compared to the benefits, current practices, recommendations made in other relevant guidelines, patient preferences and equality issues. The consensus recommendations were done through discussions in the GDG.
- The main considerations specific to each recommendation are outlined in the Evidence to Recommendation Section preceding the recommendation section of the full guideline document.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

Relevant health economic evidence for recommendations are found in the specific chapters of the full version of the original guideline document.

In addition appendices I and J of the full guideline provide details of the following original economic models:

- A cost effectiveness model comparing early and late endoscopy in people with acute upper gastrointestinal bleeding
- Time to endoscopy: statistical analysis of the UK Comparative Audit of Upper Gastrointestinal Bleeding and the use of Blood

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

The guideline was validated through two consultations.

1. The first draft of the guideline (the full guideline, National Institute for Health and Clinical Excellence [NICE] guideline, and Quick Reference Guide) were consulted with Stakeholders and comments were considered by the Guideline Development Group (GDG)
2. The final consultation draft of the Full guideline, the NICE guideline and the Information for the Public were submitted to stakeholders for final comments.

The final draft was submitted to the Guideline Review Panel for review prior to publication.

Validation Process

The guidance is subject to an eight week public consultation and feedback as part of the quality assurance and peer review the document. All comments received from registered stakeholders are responded to in turn and posted on the NICE website when the pre-publication check of the full guideline occurs.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- Appropriate management of acute upper gastrointestinal bleeding and reduced risk of death
- Acute upper gastrointestinal bleeding is a major life threatening medical emergency. However, modern management based upon endoscopic diagnosis and therapy has the potential to stop active bleeding, prevent further bleeding and save lives. Furthermore advances in drug therapies, interventional radiology and operative surgery have occurred and are used when endoscopic therapies prove unsuccessful.

Potential Harms

- Re-bleeding after liberal or delayed use of blood transfusion
- Adverse effects of drugs
- Longer hospital stay due to delayed endoscopy
- Anaesthesia/operative risks
- Development of antibiotic resistance
- Injection sclerotherapy can cause oesophageal strictures in an appreciable minority of cases, and this is not observed with band ligation.
- Acute complications from transjugular intrahepatic portosystemic shunts (TIPS) including bleeding due to capsular puncture (relatively uncommon), while the major late complication is hepatic encephalopathy
- Risk of vascular complications following discontinuation of anti-platelet drugs
- Potential increased risk of hospital acquired pneumonia and *Clostridium difficile*-associated diarrhoea with proton pump inhibitors and H₂-receptor antagonists

Refer to "Trade off between clinical benefits and harms" for each recommendation in the full version of the original guideline document for a more detailed discussion of benefits and harms.

Qualifying Statements

Qualifying Statements

- This guidance represents the view of the National Institute for Health and Clinical Excellence (NICE), which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer, and informed by the summary of product characteristics of any drugs they are considering.
- Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to avoid unlawful discrimination and to have regard to promoting equality of opportunity. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.
- The guideline will assume that prescribers will use a drug's summary of product characteristics to inform decisions made with individual patients.
- Treatment and care should take into account patients' needs, preferences and religious beliefs. People with acute upper gastrointestinal bleeding should have the opportunity to make informed decisions about their care and treatment, in partnership with their healthcare professionals. If patients do not have the capacity to make decisions, healthcare professionals should follow the Department of Health's advice on consent and the code of practice that accompanies the Mental Capacity Act. In Wales, healthcare professionals should follow advice on consent from the Welsh Government. In taking account of patients' religious beliefs in the context of blood transfusion, healthcare

professionals should follow the advice from United Kingdom (UK) Blood Transfusion and Tissue Transplantation Services.

Implementation of the Guideline

Description of Implementation Strategy

The National Institute for Health and Clinical Excellence (NICE) has developed tools to help organisations implement this guidance. These are available on the NICE Web site (<http://guidance.nice.org.uk/CG141> ; see also the "Availability of Companion Documents" field).

Key Priorities for Implementation

The following recommendations have been identified as priorities for implementation.

Risk Assessment

Use the following formal risk assessment scores for all patients with acute upper gastrointestinal bleeding:

- The Blatchford score at first assessment, and
- The full Rockall score after endoscopy

Timing of Endoscopy

Offer endoscopy to unstable patients with severe acute upper gastrointestinal bleeding immediately after resuscitation.

Offer endoscopy within 24 hours of admission to all other patients with upper gastrointestinal bleeding.

Units seeing more than 330 cases a year should offer daily endoscopy lists. Units seeing fewer than 330 cases a year should arrange their service according to local circumstances.

Management of Non-Variceal Bleeding

Do not use adrenaline as monotherapy for the endoscopic treatment of non-variceal upper gastrointestinal bleeding.

For the endoscopic treatment of non-variceal upper gastrointestinal bleeding, use one of the following:

- A mechanical method (for example, clips) with or without adrenaline
- Thermal coagulation with adrenaline
- Fibrin or thrombin with adrenaline

Offer interventional radiology to unstable patients who re-bleed after endoscopic treatment. Refer urgently for surgery if interventional radiology is not promptly available.

Management of Variceal Bleeding

Offer prophylactic antibiotic therapy at presentation to patients with suspected or confirmed variceal bleeding.

Consider transjugular intrahepatic portosystemic shunts (TIPS) if bleeding from oesophageal varices is not controlled by band ligation.

Control of Bleeding and Prevention of Re-Bleeding in Patients on Non-steroidal Anti-inflammatory Drugs (NSAIDs), Aspirin or Clopidogrel

Continue low-dose aspirin for secondary prevention of vascular events in patients with upper gastrointestinal bleeding in whom haemostasis has been achieved.

Implementation Tools

Audit Criteria/Indicators

Clinical Algorithm

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Timeliness

Identifying Information and Availability

Bibliographic Source(s)

National Institute for Health and Clinical Excellence (NICE). Acute upper gastrointestinal bleeding: management. London (UK): National Institute for Health and Clinical Excellence (NICE); 2012 Jun. 23 p. (Clinical guideline; no. 141).

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2012 Jun (reaffirmed 2014)

Guideline Developer(s)

National Guideline Centre - National Government Agency [Non-U.S.]

Source(s) of Funding

National Institute for Health and Clinical Excellence (NICE)

Guideline Committee

Composition of Group That Authored the Guideline

Guideline Development Group Members: Stephen Atkinson, Academic Clinical Fellow in Hepatology and Gastroenterology, Imperial College Healthcare NHS Trust; Mark Donnelly, Consultant Gastroenterologist, Sheffield Teaching Hospitals, Sheffield; Katharina Dworzynski, Senior Research Fellow, NCGC; Richard Forbes-Young, Advanced Nurse Practitioner, GI Unit, Western General Hospital, Edinburgh; Carlos Gomez, Intensivist, St Mary's Hospital, London; Daniel Greer, Pharmacist Lecturer/Practitioner, University of Leeds/Leeds Teaching Hospitals, Leeds; Lina Gulhane, Information Scientist Lead/Senior Information Scientist, NCGC; Kenneth Halligan, Patient/Carer Representative, Liverpool; Markus Hauser, Consultant Physician in Acute Medicine, Cheltenham General Hospital, Cheltenham; Bernard Higgins, Clinical Director, NCGC; Panos Kefalas, Senior Project Manager, NCGC (until January 2011); Amy Kelsey, Project Manager, NCGC; Phillipe Laramée, Health Economist, NCGC (until February 2011); Simon McPherson, Consultant Vascular and Interventional Radiologist, United Leeds Teaching Hospitals Trust, Leeds; Mimi McCord, Patient/Carer Representative, Chichester; Kelvin Palmer (*GDG Chair*), Consultant Gastroenterologist, GI Unit, Western General Hospital, Edinburgh; David Patch, Consultant Hepatologist, Royal Free Hospital, London; Vicki Pollit, Acting Senior Health Economist, NCGC; Joseph Varghese, Consultant Surgeon, Royal Bolton Hospital NHS Foundation Trust, Bolton; Mark Vaughan, GP, Meddygfa Avenue Villa Surgery, Llanelli, Wales; David Wonderling, Health Economics Lead, NCGC

Financial Disclosures/Conflicts of Interest

At the start of the guideline development process all Guideline Development Group (GDG) members declared interests including consultancies, fee-paid work, share-holdings, fellowships and support from the healthcare industry. At all subsequent GDG meetings, members declared arising conflicts of interest, which were also recorded. Members were either required to withdraw completely or for part of the discussion if their declared interest made it appropriate.

The details of declared interests and the actions taken are shown in Appendix B of the full version of the original guideline document (see the "Availability of Companion Documents" field).

Guideline Status

This is the current release of the guideline.

The National Institute for Health and Clinical Excellence (NICE) reaffirmed the currency of this guideline in 2014.

Guideline Availability

Electronic copies: Available from the [National Institute for Health and Clinical Excellence \(NICE\) Web site](#) .

Availability of Companion Documents

The following are available:

- Acute upper gastrointestinal bleeding. Full guideline. London (UK): National Institute for Clinical Excellence (NICE); 2012 Jun. 285 p. (Clinical guideline; no. 141). Electronic copies: Available in Portable Document Format (PDF) from the [National Institute for Health and Clinical Excellence \(NICE\) Web site](#) .
- Acute upper gastrointestinal bleeding. Appendices. London (UK): National Institute for Clinical Excellence (NICE); 2012 Jun. 627 p. (Clinical guideline; no. 141). Electronic copies: Available in PDF from the [NICE Web site](#) .
- NICE Pathways. Acute upper gastrointestinal bleeding. London (UK): National Institute for Clinical Excellence (NICE); 2012 Jun. Electronic copies: Available from the [NICE Web site](#) .
- Acute upper gastrointestinal bleeding. Clinical audit tools. National Institute for Health and Clinical Excellence (NICE); 2012 Jun. Various p. (Clinical guideline; no. 141). Electronic copies: Available from the [NICE Web site](#) .
- Acute upper gastrointestinal bleeding. Electronic audit tools. National Institute for Health and Clinical Excellence (NICE); 2012 Jun. (Clinical guideline; no. 141). Electronic copies: Available from the [NICE Web site](#) .

- Acute upper gastrointestinal bleeding. Costing report. National Institute for Health and Clinical Excellence (NICE); 2012 Jun. 25 p. (Clinical guideline; no. 141). Electronic copies: Available in PDF from the [NICE Web site](#) .
- Acute upper gastrointestinal bleeding. Baseline assessment tool. National Institute for Health and Clinical Excellence (NICE); 2012. (Clinical guideline; no. 141). Electronic copies: Available from the [NICE Web site](#) .
- The guidelines manual 2009. London (UK); National Institute for Health and Clinical Excellence (NICE); 2009 Jan. Electronic copies: Available from the [NICE Archive Web site](#) .
- Acute upper gastrointestinal bleeding. Evidence update. National Institute for Health and Clinical Excellence (NICE); 2014 Aug. 16 p. Electronic copies: Available from the [NICE Web site](#) .

Patient Resources

The following is available:

- Acute upper gastrointestinal bleeding. Understanding NICE guidance. Information for people who use NHS services. London: National Institute for Health and Clinical Excellence (NICE); 2012 Jun. 8 p. Electronic copies: Available in Portable Document Format (PDF) from the [National Institute for Health and Clinical Excellence \(NICE\) Web site](#) .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This summary was completed by ECRI Institute on July 26, 2012. The currency of the guideline was reaffirmed by the developer in 2014 and this summary was updated by ECRI Institute on November 4, 2014. This summary was updated by ECRI Institute on February 15, 2017 following the U.S. Food and Drug Administration advisory on general anesthetic and sedation drugs.

The National Institute for Health and Clinical Excellence (NICE) has granted the National Guideline Clearinghouse (NGC) permission to include summaries of their clinical guidelines with the intention of disseminating and facilitating the implementation of that guidance. NICE has not yet verified this content to confirm that it accurately reflects that original NICE guidance and therefore no guarantees are given by NICE in this regard. All NICE clinical guidelines are prepared in relation to the National Health Service in England and Wales. NICE has not been involved in the development or adaptation of NICE guidance for use in any other country. The full versions of all NICE guidance can be found at [www.nice.org.uk](#) .

Copyright Statement

This NGC summary is based on the original guideline, which is subject to the guideline developer's copyright restrictions.

Disclaimer

NGC Disclaimer

The National Guideline Clearinghouse[®] (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public or private organizations, other government agencies, health care organizations or plans, and similar entities.

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the [NGC Inclusion Criteria](#).

NGC, AHRQ, and its contractor ECRI Institute make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines

represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI Institute, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.